Implantable Infusion Pumps

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Policy
Blue Cross and Blue Shield of Kansas City (Blue KC) will provide coverage for implantable infusion pumps when it is determined to be medically necessary because the criteria shown below are met.

When Policy Topic is covered
Implantable infusion pumps are considered medically necessary when used to deliver drugs having FDA approval for this route of access and for the related indication for the treatment of:

- Cancer in the following situations:
  - Primary liver cancer (intrahepatic artery injection of chemotherapeutic agents);
  - Metastatic colorectal cancer where metastases are limited to the liver (intrahepatic artery injection of chemotherapeutic agents);
  - Primary epithelial ovarian cancer (intraperitoneal infusion as component of chemotherapy)
- Severe, chronic, intractable pain (intravenous, intrathecal, and epidural injection of opioids), following a successful temporary trial of opioid or non-opioid analgesics by the same route of administration as the planned treatment. A successful trial is defined as greater than 50% reduction in pain following implementation of treatment; and
- Severe spasticity of cerebral or spinal cord origin in patients who are unresponsive to or who cannot tolerate oral baclofen therapy (intrathecal injection of baclofen).

When Policy Topic is not covered
Implantable infusion pumps are considered investigational for all other uses (e.g., chemotherapy for patients with head and neck cancers or gastric cancer, heparin for thromboembolic disease, insulin for diabetes, antibiotics for osteomyelitis).

Considerations
Implantable infusion pumps should not be confused with the type of portable pumps used to infuse short-term analgesia directly into a post operative wound site. These types of pumps are external, with the tip of the catheter sutured into place near the surgical site.

Description of Procedure or Service
Implantable infusion pumps can provide long-term drug infusion at constant or variable rates. Primary uses are delivery of chemotherapy agents and analgesics; several devices are commercially available.

Background
An implantable infusion pump is intended to provide long-term continuous or intermittent drug infusion. Possible routes of administration include intravenous, intra-arterial, subcutaneous, intraperitoneal, intrathecal, and epidural. The implantable infusion pump is surgically placed in a subcutaneous pocket under the infraclavicular fossa or in the abdominal wall, and a catheter is threaded into the desired position. Intrathecal and epidural catheter positions are both intraspinal; however, the intrathecal position is located in the subarachnoid space, which is past the epidural space and dura mater and through the theca of the spinal cord.
A drug is infused over an extended period of time and may be delivered at a constant or variable rate by calibrating the implantable infusion pump per physician specifications. The drug reservoir may be refilled as needed by an external needle injection through a self-sealing septum in the implantable infusion pump. Bacteriostatic water or physiological saline is often used to dilute drugs. A heparinized saline solution may also be used during an interruption of drug therapy to maintain catheter patency.

The driving mechanisms may include peristalsis, fluorocarbon propellant, osmotic pressure, piezoelectric disk benders, or the combination of osmotic pressure with an oscillating piston.

**Regulatory Status**

Several implantable infusion pumps have been approved by the U.S. Food and Drug Administration (FDA) through the premarket approval process, including, but not limited to, the Medtronic SynchroMed® (Fridley, MN) family of pumps; the Medtronic IsoMed® infusion system (Minneapolis, MN); the Flowonix™ Prometra® programmable pump (Mount Olive, NJ); and Shiley Infusaid® pumps (Norwood, MA). In August 2012, FDA approved the MedStream™ Programmable Infusion System (Codman and Shurtleff – a division of DePuy), which includes an implantable pump, for intrathecal delivery of baclofen in patients with spasticity.

**Rationale**

This original policy was based on a search of the MEDLINE database through December 1995. The policy was on “no further review” status from 2003 until 2010, at which time it returned to active status. Since 2010, literature searches have been performed regularly, most recently for the period September 2012 through August 2013. Following is a summary of the key literature published to date.

**Chemotherapy for Cancer Patients**

*Primary liver cancer*

No randomized controlled trials (RCTs) have evaluated whether hepatic arterial infusion of chemotherapy in patients with primary liver cancer improves health outcomes. A 2013 comparative effectiveness review by the Agency for Healthcare Research and Quality (AHRQ) evaluated local therapies for unresectable primary hepatocellular carcinoma in patients ineligible for surgical resection or transplantation. (1) Treatments reviewed included ablative therapies (eg, radiofrequency ablation), radiotherapy (eg, intraluminal brachytherapy), and embolization (eg, transarterial embolization either with [TACE] or without [TAE] chemotherapy). Although TACE delivers chemotherapy and embolic materials through hepatic arterial infusion, this procedure generally is performed by an interventional radiologist and does not require implantation of an infusion pump. Thus, this AHRQ report does not address the use of implantable infusion pumps for delivery of chemotherapy for primary liver cancer.

Several case series were identified. Most recently, Jarnagin et al. (2009) reported on 34 patients with unresectable primary liver cancer who received hepatic arterial infusion of floxuridine and dexamethasone. (2) Sixteen of 34 patients (47%) had a partial response to treatment. Median survival was 29.5 months; the 2-year survival rate was 67%. In addition, Smith et al. (1984) studied 11 patients and found a complete response to chemotherapy in 1 patient and partial responses in 6 patients. (3) Atiq et al. found a partial response in 4 of 10 patients (40%) with unresectable liver cancer treated with intrahepatic chemotherapy delivered through an implantable pump. (4)

This evidence is limited but suggests that some patients, with limited alternative treatment options, may benefit from arterial infusion of chemotherapy.

*Liver metastases from colorectal cancer*

A 2012 AHRQ comparative effectiveness review evaluated local hepatic therapies for colorectal cancer metastases in patients ineligible for systemic chemotherapy. (5) Like the AHRQ review mentioned
above, local therapies included ablation, radiotherapy, and embolization. Four case series of chemotherapy delivered via hepatic artery infusion by an indwelling pump were identified. Two retrospective case series assessed a total of 67 patients who were refractory to systemic chemotherapy, and 2 case series assessed a total of 36 patients who received concomitant systemic chemotherapy. Infused chemotherapies were mitomycin plus gemcitabine or 5-fluorouracil; systemic chemotherapy regimens varied. Median overall survival was 9.7 months and 6.7 months in the refractory group, and 30.1 months and 22.0 months in the systemic chemotherapy group. Grade 3 adverse events attributed to hepatic artery infusion included leukocytopenia, hyperbilirubinemia, hypersensitivity reaction, and neuropathy. This evidence was considered insufficient to form any conclusion about the comparative benefits (e.g., overall survival, quality of life) or harms (ie, adverse events) of hepatic artery infusion for these patients.

For patients who are eligible for systemic chemotherapy, a 2009 Cochrane review compared hepatic arterial infusion versus systemic chemotherapy in patients with unresectable liver metastases from colorectal cancer. Ten RCTs that evaluated a total of 1277 patients were included. Nine of these provided data on tumor response. The response rate was significantly higher in the hepatic arterial infusion group (198 of 461, 43%) than the systemic chemotherapy group (81 of 440, 18%). The pooled risk ratio (RR) was 2.26 (95% confidence interval [CI], 1.80 to 2.84). However, there was not a significantly higher survival rate associated with hepatic arterial infusion chemotherapy. The mean weighted median overall survival times were 15.9 months with hepatic arterial infusion chemotherapy and 12.4 months with systemic chemotherapy (pooled hazard ratio [HR]=0.90; 95% CI, 0.76-1.07). Adverse effects and quality-of-life outcomes were not reported.

This evidence suggests that arterial infusion of chemotherapy improves response rates for patients with colorectal cancer metastatic to the liver compared to systemic chemotherapy. The impact on survival is uncertain.

**Head and neck cancers**

Several studies have evaluated interventions that combine radiotherapy and concomitant intra-arterial cisplatin (known as RADPLAT) on patients with head and neck cancer. These studies used intra-arterial delivery of cisplatin via an intra-arterial catheter rather than an implantable pump. Although an implantable infusion pump was not used, the principle of treatment is similar, so that these studies have some relevance to the evaluation of infusion pumps.

In 2006, Hoebers et al. in The Netherlands randomized patients with stage III or IV head and neck squamous cell carcinoma to radiotherapy with standard intravenous (IV) cisplatin (n=21) or high-dose intra-arterial cisplatin (n=14). Rates of acute mucositis and hematological toxicity did not differ significantly between groups; however, there was a higher rate of acute renal toxicity in the IV group (30%) compared to the intra-arterial group (0%). Over 2 years, there were no significant differences between treatment groups in locoregional control of disease, disease-free survival, or overall survival.

A study by Ackerstaff et al. (2009) examined 17 quality-of-life scales at several time points after treatment with radiotherapy with intravenous or intra-arterial cisplatin. The study included 207 patients with inoperable advanced head and neck cancer. The only statistically significant difference between groups was in the nausea/vomiting scale at 7 weeks, at which time the incidence of symptoms was higher in the intravenous compared to the intra-arterial group. Otherwise, quality-of-life symptoms were similar in the 2 groups.

Evidence from 2 RCTs did not find a clear advantage of intra-arterial chemotherapy delivered via an intra-arterial catheter compared to IV chemotherapy in combination with radiotherapy for patients with head and neck cancer. Therefore, it is not likely that similar agents delivered via an implantable infusion pump would improve outcomes.

**Primary epithelial ovarian cancer**
A 2011 Cochrane review examined literature on whether an intraperitoneal (IP) component of chemotherapy improves ovarian cancer outcomes compared to intravenous chemotherapy-only. (9) Nine RCTs with a total of 2119 patients were identified; 6 trials were considered high quality. In a pooled analysis of data from 8 trials, there was a significantly lower rate of mortality with an IP component of chemotherapy compared to no IP component (HR=0.81; 95% CI, 0.72 to 0.90). Moreover, a pooled analysis of data from 5 trials found that an IP component of chemotherapy was associated with a significantly longer disease-free interval (HR=0.78; 95% CI, 0.70 to 0.86). However, an IP component of chemotherapy was associated with significantly more adverse effects (e.g., infection, fever, pain, and gastrointestinal symptoms). For example, a pooled analysis of 3 trials found a significantly higher infection rate when there was an IP component of chemotherapy compared to IV-only chemotherapy (RR=3.34; 95% CI, 2.06 to 5.43).

An example of one of the individual RCTs is a high-quality RCT with a relatively large number of patients published by Markman et al. in 2001. (10) This was a multicenter study conducted in the United States and included women diagnosed with stage III epithelial ovarian cancer who entered the study within 6 weeks of surgery. Patients were randomized to receive either standard dose IV cisplatin/paclitaxel for 6 courses or 2 cycles of moderately high-dose carboplatin, followed by 6 courses of IV paclitaxel and intraperitoneal cisplatin. A total of 523 patients entered the trial, and 61 (12%) were subsequently found to be ineligible for reasons including the wrong stage of cancer or inadequate surgery. Of the remaining 462 eligible patients, 227 were in the IV chemotherapy-only group and 235 were in the IP chemotherapy-component group. At the time of data analysis, 103 of 227 patients (45.4%) in the IV-only group and 126 of 235 (53.6%) in the IP chemotherapy-component group were still alive. Improvement in survival with IP chemotherapy was of borderline statistical significance (RR=0.81; 95% CI, 0.65 to 1.00). Progression-free survival was significantly longer in the IP chemotherapy-component group compared to the IV chemotherapy-only group (median time to recurrence: 27.9 months vs 22.2 months, respectively, p=0.01). Several adverse events occurred more commonly in the IP chemotherapy-component group than in the IV chemotherapy-only group. These included grade 3-4 gastrointestinal events (37% vs 17%, respectively) and platelet toxicity (49% vs 3%, respectively). Two patients in each group died of causes considered to be related to chemotherapy.

Evidence from multiple RCTs, including some of high-quality, and systematic reviews, indicates that intraperitoneal chemotherapy for patients with primary epithelial ovarian cancer has a significant impact on progression-free survival and likely also improves overall survival. This benefit is accompanied by an increased risk of adverse effects with intraperitoneal infusions, including infections, pain, and gastrointestinal symptoms.

**Gastric cancer**

A 2011 systematic review examined RCTs and observational studies on intraperitoneal chemotherapy used to treat gastric cancer. (11) The authors identified 14 studies: 2 RCTs, 2 case-control studies, and 10 single cohort studies. One of the RCTs compared groups of patients who did and did not receive intraperitoneal taurolidine following tumor resection and did not find statistically significant differences in outcomes. The other RCT (n=118) found a significantly higher rate of survival in patients who received either IP chemotherapy plus intraoperative peritoneal lavage or IP chemotherapy only in addition to surgery versus surgery only. (Additionally, all patients in the second study received adjuvant oral 5-fluorouracil derivatives for 2 years.) The authors of the systematic review recommended that future studies evaluate preoperative or intraoperative IP chemotherapy in association with systemic chemotherapy. This evidence on intraperitoneal chemotherapy for treating gastric cancer is insufficient to determine whether health outcomes are improved.

**Pain**

**Cancer pain**
One systematic review of the literature was identified; it was published in 2010 by Myers et al. They identified 12 RCTs on intraspinal techniques for managing pain in cancer patients; studies were required to report pain as an outcome measure using a validated scale. The investigators did not identify the type or types of cancer addressed in individual studies and did not pool study findings. Two RCTs specifically addressed implantable infusion pumps. One compared intrathecal morphine delivered via an implantable infusion pump plus medical management (n=101) to medical management alone (n=99) in patients with refractory cancer pain. The difference between groups in clinical success (defined as a minimum 20% reduction in pain score and a minimum 20% reduction in drug toxicity at 4 weeks) reached borderline statistical significance, favoring the implantable pump group over the control group (85% vs 71%, respectively, p=0.05). The proportion of patients who experienced a minimum 20% pain score reduction was 52% in the implantable pain pump group and 39% in the control group; this was not a statistically significant difference (p=0.55). The other RCT on implantable pumps compared epidural morphine delivered as a continuous infusion by the Infusaid pump to intermittent delivery by a Port-a-Cath® (Deltec, Saint Paul, MN). The 2 groups did not differ significantly in their pain scores; scores were low in both groups, and the trial, which had only 29 participants, was likely underpowered. The evidence from this systematic review indicates that intraspinal techniques may be appropriate for select cancer patients with intractable cancer pain but there is a shortage of high-quality RCTs.

Noncancer pain

In 2013, the American Society of Interventional Pain Physicians (Falco et al.) published a systematic review of intrathecal infusion for the treatment of chronic noncancer pain. The outcome of interest was pain relief, defined as a minimum 50% reduction of pain in at least 40% of patients, or a minimum 3-point reduction in pain scores. Both short-term (less than 12 months) and long-term (12 months or longer) outcomes were considered. Twenty-eight studies were identified, but 21 were excluded for not meeting one or more inclusion criteria (eg, outcomes not related to pain relief; sample size less than 50; minimum quality assessment). All 7 included studies were retrospective or prospective cohort studies. Six studies that each reported short-term (668 patients) or long-term (637 patients) pain outcomes indicated reduced pain with intrathecal opioids. The authors concluded that evidence for intrathecal opioid infusion in chronic noncancer pain is limited. Suggested contraindications to intrathecal opioid therapy (eg, active infection) and indications to proceed with therapy (eg, oral opioid therapy contraindicated) are provided.

In 2009, Patel et al. published a systematic review of intrathecal infusion pumps used to treat chronic noncancer pain. Included studies evaluated an intrathecal device (programmable or fixed infusion rate), stated a specific indication and the drug that was injected, followed patients for at least 12 months, and included at least 25 patients. In addition, the investigators rated study quality; included studies scored at least 50 out of 100 on a methodologic quality scale. The primary outcome of interest to the systematic review was pain relief. A total of 15 studies on intrathecal infusion for noncancer pain were identified; however, 6 did not have sufficient follow-up, 4 included fewer than 25 patients, and 1 had unacceptably low quality, leaving 4 eligible studies. All of the studies were observational and involved intrathecal opioid administration; sample sizes ranged from 69 to 120. Most patients experienced lumbospinal pain. Two of the 4 studies showed positive results for pain relief, one study had negative results, and results were unavailable for the fourth study. The authors of the systematic review acknowledged the paucity of literature and lack of RCTs. Using the grading system developed by Guyatt et al., the authors concluded that a 1C recommendation for the use of intrathecal infusion systems in chronic noncancer pain was appropriate; that is, a strong recommendation based on low-quality or very low-quality evidence in which the benefits outweigh the risks and the recommendation may change when higher quality evidence becomes available.

In 2012, Hamza et al. published a 36-month prospective cohort study of low-dose intrathecal (IT) opioids for chronic nonmalignant pain using the Synchromed II programmable pump. Sixty-one patients with severe intractable pain who had failed multiple lines of pain therapy and were referred for IT treatment underwent a blinded trial of IT opioids. Three patients who experienced pain relief in response to saline were excluded. Mean age of the 58 included patients was 59±14 years, and mean
duration of symptoms was 6±2 years. Pain syndromes were failed back surgery syndrome in 60% of patients, chronic low back pain in 28%, and chronic complex regional pain syndrome, abdominal pain, or pelvic pain in 12%. All patients were weaned from opioids for 7 to 10 days before pump implantation and participated in a 12-week physical therapy program commencing at 8 weeks postimplant. At 36 months, there was a 55% reduction from baseline worst pain score (from 8.91 to 4.02 on the Brief Pain Inventory [BPI] 0-10 scale; p=0.012) and a 54% reduction from baseline average pain score (from 7.47 to 3.41; p<0.001). Improvements in physical function and behavior (mood, relations, and sleep) as measured by the BPI also were statistically significant. Mean IT opioid dose increased 11% from 1.4 to 1.6 morphine equivalents daily. Mean oral opioid dose decreased 97% from 129 to 4 morphine equivalents daily. Adverse events were reported to be mild and limited (wound infection and pruritus in 3 patients [5%] each; peripheral edema and seroma in 2 patients [3%] each).

Several additional case series were identified in recent literature searches. In 2010, Atli et al. published a single-center study conducted in the U.S.(17) This was a retrospective review of 57 patients referred for pain management who received an implanted intrathecal infusion pump. Twenty-eight of the 57 patients (49%) had failed back surgery syndrome, 16 (28%) had neuropathic pain, and the remaining 13 (23%) had a variety of diagnoses. Preservative-free opioid (usually morphine) was infused, and patients also could receive oral opioid; adjustments in dosage could be made at any time. Forty-nine of 57 patients (86%) completed the 3-year follow-up. At the time of the first pump refill (3-6 months), 23 of 49 study completers (47%) reported having a 50% or greater reduction in pain from baseline, as measured on a 10-point visual analogue scale. The proportion of responders decreased over time; at the 3-year follow-up, 9 of 49 patients (18%) had a 50% or greater reduction in pain from baseline. These 9 patients represented 39% of those who met the 50% reduction threshold at the first refill. The use of oral opioids was significantly less at the 1- and 3-year follow-ups than at baseline (p values not reported). Mean baseline oral opioid dose in morphine equivalents was 184 mg/24 hours. At 1 and 3 years, mean oral doses were 44 mg/24 hours and 58 mg/24 hours, respectively. At 3 years, 12 of 49 patients (25%) had ceased all oral opioid use. In contrast, mean dose of intrathecal opioids significantly increased during follow-up compared to the dose at discharge after pump implantation. The mean dose was 6.5 mg/24 hours at discharge; 9.3 mg/24 hours at 1 year; and 12.2 mg/24 hours at 3 years. Complications occurred in 10 of 57 patients (17.5%); these included 5 infections, 3 catheter revisions, 2 seromas at the pump site, and 2 intrathecal granulomas. Another retrospective case series conducted in the U.S. and published in 2011 included 126 noncancer intractable pain patients.(18) Patients received intrathecal opioids only (n=72) or opioids and bupivacaine (n=54). Outcomes were evaluated 12 months after pump implantation. Pain intensity was assessed using an 11-point numeric rating scale (NRS) in which 0=no pain and 10=the worst imaginable pain. In the group that began with opioids only, mean pain intensity score decreased significantly from 7.42 (standard deviation [SD]=2.1) at baseline to 5.85 (SD=2.8) at 12 months, p<0.001. In the opioid plus bupivacaine group, the mean pain intensity score decreased from 7.35 (SD=2.1) at baseline to 5.03 (SD=2.4) at 12 months, p<0.001.

In 2012, Duarte et al. in the U.K. published a case series with long-term follow-up on 20 patients with chronic nonmalignant pain who received intrathecal delivery of opioid analgesics.(19) Patients were followed for a mean of 13.5 years (range, 10.4 to 17.9 years). At 4- and 13-year assessments, outcomes were significantly improved compared to baseline. However, outcomes did not significantly improve between 4 and 13 years. For example, mean pain intensity (measured on an 11-point scale in which 0 represents no pain and 10 represents the worst pain) was 8.65 (SD=0.29) at baseline, 4.95 (SD=0.53) at 4 years posttreatment, and 5.30 (SD=0.35) at 13 years posttreatment. Similarly, mean quality-of-life score (0 represents no interference with quality of life and 10 represents maximum interference) was 8.45 (SD=0.49) at baseline, 4.95 (SD=0.69) at 4 years, and 4.45 (SD=0.48) at 13 years.

In summary, evidence on the use of infusion pumps for chronic, noncancer pain consists of numerous uncontrolled observational studies. These studies, which are limited methodologically, report that pain and quality of life is improved with the use of infusion pumps.

Severe Spasticity
The evidence base consists of case series and a systematic review of case series. The systematic review, published in 2011 by Pin et al., focused on intrathecal baclofen therapy for spasticity and/or dystonia of cerebral origin. The authors identified 16 uncontrolled studies with a total of 227 participants. All studies were judged to be low quality. Most outcomes were intermediate measures (i.e., at the level of body structures or functions), such as range of motion and muscle strength; several studies used objective outcomes (e.g., motor function at the level of activities or participation as assessed by the Gross Motor Function Measure, laboratory-based gait analysis, or gait assessment tools). The authors’ interpretation of the studies was that they showed a higher rate of benefit with intrathecal baclofen therapy in patients who were already ambulatory. Adverse events were not consistently defined and reported but appeared to be common. One study that used objective outcomes was published in 2011 by Motta et al. in Italy. This study found a statistically significant increase in the Gross Motor Function Measure (GMFM) score after 1 year. Median GMFM score (as a percentage of maximum score) in 30 cerebral palsy patients with spasticity who received intrathecal baclofen increased from 65.0 to 69.4 (p=0.004).

In 2011 (after the Pin et al. literature search), Morton et al. in the U.K. published findings of a nonrandomized controlled study of intrathecal baclofen therapy in nonambulant children with severe spastic cerebral palsy. Patients who responded to a one-time test dose of 50 mg intrathecal baclofen were fitted for a pump and placed on a waiting list for surgery. The investigators compared patients who had been on the waiting list between 6 to 12 months (group 1, n=18) to patients who had undergone surgery (group 2, n=20). Mean time between baseline and outcome assessment was 8.5 months in group 1 and 9.5 months in group 2. There was no statistically significant difference between the 2 groups in the primary outcome measure, the Pediatric Evaluation of Disability Inventory (PEDI). The authors noted, however, that given the small number of patients recruited, the study was underpowered to detect clinically significant differences between groups on this outcome. Several secondary outcomes favored group 2, including scores on the Modified Ashworth Scale (difference between groups 1.7, p=0.008), scores on the Penn Spasm Scale (difference between groups, -1.3, p=0.001) and the range-of-motion score (difference between groups, 8.3, p=0.005).

A small 2012 study compared mode of administration of intrathecal baclofen in 38 adults with muscle hypertonia due to brain injury or spinal cord disorder who were receiving intrathecal baclofen. Pumps were programmed to deliver a single daily bolus of baclofen with low background continuous dose (intervention group) or a continuous equivalent daily dose (controls). For patients receiving 75 to 85 mg of baclofen daily, a neurophysiologic measure of spasticity (H-reflex in the soleus [calf] muscle) improved statistically significantly more in the intervention group than in controls. For patients receiving 100-150 mg of baclofen daily, the difference between groups was not statistically significant.

Evidence from case series and nonrandomized, comparative studies report improvements in spasticity for patients treated via implantable infusion pumps. However, there is a lack of high-quality RCTs to confirm this benefit.

**Implanted Infusion Pumps for Other Indications**

No systematic reviews, meta-analyses, or large RCTs on the use of implanted infusion pumps for any additional indication were identified.

**Ongoing Clinical Trials**

**SISTERS: Spasticity in Stroke Study (NCT01032239):** This RCT compares intrathecal baclofen therapy to best medical treatment for patients with severe spasticity for at least 6 months following stroke. The primary outcome is change in the Ashworth scale. Estimated enrollment is 88 patients, and the expected date of completion is January 2015.

**Secondary Debulking Surgery with and without Hyperthermic Intraperitoneal Chemotherapy in Stage III Ovarian Cancer (NCT00426257):** This open-label RCT compares secondary debulking with secondary
debunking plus intraperitoneal chemotherapy in patients with stage III ovarian cancer. The primary outcome is duration of recurrence-free survival. Estimated enrollment is 280 patients, and the expected date of study completion is December 2013.

**Phase 3 Trial Evaluating Hyperthermic Intraperitoneal Chemotherapy in Upfront Treatment of Stage IIIC Epithelial Ovarian Cancer (CHORINE) (NCT01628380):** This RCT compares cytoreductive surgery plus chemotherapy with an intraperitoneal component with cytoreductive surgery only in patients with stage IIIc epithelial ovarian cancer. The trial is conducted in Italy and is sponsored by Bergamo Hospital. The primary outcome is disease-free survival; overall survival is a secondary outcome. Estimated enrollment is 94 patients, and the expected date of study completion is July 2016.

**Regional Versus Systemic Chemotherapy in the Treatment of Unresectable Pancreatic Cancer (NCT01665625):** This open-label RCT compares systemic gemcitabine therapy to continuous regional delivery of gemcitabine using an implanted percutaneous left subclavian artery port-catheter drug delivery system in patients with inoperable pancreatic carcinoma. The primary outcome is overall survival. Estimated enrollment is 90 patients, and the expected date of completion is February 2016.

**Clinical Input Received through Physician Medical Societies and Academic Medical Centers**

In response to requests, input was received through 1 Physician Specialty Society and 3 Academic Medical Centers while this policy was under review in 2012. Although the various Physician Specialty Societies and Academic Medical Centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the Physician Specialty Societies or Academic Medical Centers, unless otherwise noted. Clinical input focused on implantable infusion pumps for treating patients with cancer; other potential indications were not addressed. There was consensus that implantable infusion pumps may be considered medically necessary for treating patients with primary liver cancer, metastatic colorectal cancer and epithelial ovarian cancer. Reviewers from 3 of 4 organizations disagreed that implantable infusion pumps are medically necessary for providing chemotherapy in patients with head and neck cancer. There was consensus among reviewers that implantable infusion pumps are investigational for all other uses in cancer patients e.g., chemotherapy for patients with gastric cancer.

**Summary**

There is a large body of evidence on the use of infusion pumps, but the quality of the literature varies by condition. For patients with primary liver cancer, evidence is limited. However, these patients have few alternative treatment options, and some may benefit from hepatic arterial infusion of chemotherapy. Clinical input supported the use of implantable infusion pumps for this indication, which is therefore considered medically necessary.

For patients with colorectal cancer metastatic to the liver, a 2009 meta-analysis of randomized controlled trials found that hepatic arterial infusion of chemotherapy with implanted infusion pumps improves tumor control. For women with primary epithelial ovarian cancer, evidence from randomized controlled trials (RCTs) and a systematic review of RCTs indicates that an intraperitoneal infusion of chemotherapy can lead to improved survival and progression-free survival compared to intravenous chemotherapy only. Benefits of intraperitoneal chemotherapy must be weighed against the risk of adverse events, which has been found to be higher with an intraperitoneal component of chemotherapy. For patients with chronic cancer pain, a systematic review of RCTs concluded that pain symptoms were reduced in patients who used an infusion pump. For these 3 indications, evidence is sufficient to conclude that the use of an implantable infusion pump improves outcomes and therefore may be considered medically necessary.

There is insufficient evidence suggesting that chemotherapy delivered through implantable infusion pumps improves health outcomes for patients with head and neck cancer or gastric cancer. Clinical
input did not support use of this technology for these types of cancer. Thus, these indications are considered investigational.

For patients with intractable, noncancer pain, the evidence consists of uncontrolled studies that report improvements in pain and quality of life following the use of an implantable infusion pump. Additionally, guidelines from specialty societies support the use of infusion pumps for this indication. For patients with severe spasticity, evidence from case series and nonrandomized controlled studies reports improvements in symptoms, and there is support from specialty society guidelines for use in spasticity. Because of the strong rationale for use, the suggestive evidence, and the support from clinical guidelines, infusion pumps may be considered medically necessary for chronic, intractable noncancer pain and for severe spasticity.

**Practice Guidelines and Position Statements**

**Cancer pain**

Current guidelines (2013) from the National Comprehensive Cancer Network include the following statements:

- “Placement of a hepatic arterial port or implantable pump during surgical intervention for liver resection with subsequent infusion of chemotherapy directed to the liver metastases through the hepatic artery (e.g., HAI) remains an option.”
- “The panel recommends that systemic cytotoxic chemotherapy (single agent or combination), intra-arterial chemotherapy, as well as the combination of cytotoxic chemotherapy and radiation therapy be given to patients with unresectable HCC only in the context of a clinical trial.”
- The 2013 information summaries from the National Cancer Institute (NCI) state the following:
  - For patients with Stage IV and recurrent colon cancer with liver metastases, hepatic intra-arterial chemotherapy with floxuridine has had higher overall response rates but not a consistent improvement in survival when compared to systemic chemotherapy.
  - For patients with localized and locally advanced unresectable adult primary liver cancer, infusion of chemotherapeutic agents with a subcutaneous portal or implantable pump via a catheter placed in the hepatic artery is described as a standard treatment option.

**Noncancer pain**

Publications from the American Society of Interventional Pain Physicians include:

- Evidence-based guidelines (updated in 2009) on interventions for managing chronic spinal pain. The guidelines state that there is strong evidence to support the use of implantable intrathecal drug administration systems with proper patient selection criteria.
- A 2013 systematic review of intrathecal infusion systems for long-term management of chronic noncancer pain, reviewed above. The authors concluded that the evidence for intrathecal opioid infusion in this setting is limited. Intrathecal opioid therapy may be indicated in select patients, eg, those with contraindications to oral opioid therapy.

**Spasticity**

In July 2012, Britain’s National Institute for Health and Care Excellence (NICE) published an evidence-based clinical guideline on the management of spasticity in children and young people with nonprogressive brain disorders. Intrathecal baclofen may be considered for children and young people with spasticity or dystonia that causes difficulty with pain or muscle spasms; posture or function; or self-care or ease of care by parents or caregivers. Additional recommendations include:

- Consideration of potential adverse effects of reducing spasticity when spasticity may support function, eg, by compensating for muscle weakness.
- A trial of intrathecal baclofen to assess efficacy and adverse events before deciding to implant the intrathecal pump.
In 2010, the European Working group for Spasticity in Children published a consensus statement on the use of intrathecal baclofen therapy in children with spasticity. (30) For children with spasticity that interferes with function or quality of life, they recommended conservative treatment and a trial of oral medication before use of a pump to deliver intrathecal baclofen. They also recommended individuation of treatment and involvement of parents and caregivers. The group received an unrestricted educational grant from Medtronic (Minneapolis, MN).

**Medicare National Coverage**

Medicare provides coverage for implantable infusion pumps for the following indications (31):

1. Intra-arterial infusion of 5-FUdR (5-fluorouracil deoxyribose) for the treatment of liver cancer for patients with primary hepatocellular carcinoma or Duke's Class D colorectal cancer, in whom the metastases are limited to the liver and where the disease is unresectable or the patient refuses surgical excision of the tumor.

2. Administration of antispasmodic drugs intrathecally (eg, baclofen) to treat chronic intractable spasticity in patients who have proven unresponsive to less invasive medical therapy as determined by the following criteria:
   - As indicated by at least a 6-week trial, the patient cannot be maintained on noninvasive methods of spasm control, such as oral antispasmodic drugs, either because these methods fail to control adequately the spasticity or produce intolerable side effects, and
   - Prior to pump implantation, the patient must have responded favorably to a trial intrathecal dose of the antispasmodic drug.

3. Administration of opioid drugs (eg, morphine) intrathecally or epidurally for treatment of severe chronic intractable pain of malignant or nonmalignant origin in patients who have a life expectancy of at least 3 months and who have proven unresponsive to less invasive medical therapy as determined by the following criteria:
   - The patient's history must indicate that he/she would not respond adequately to noninvasive methods of pain control, such as systemic opioids (including attempts to eliminate physical and behavioral abnormalities that may cause an exaggerated reaction to pain); and
   - A preliminary trial of intraspinal opioid drug administration must be undertaken with a temporary intrathecal/epidural catheter to substantiate adequately acceptable pain relief and degree of side effects (including effects on the activities of daily living) and patient acceptance.

4. Other uses of implanted infusion pumps if:
   - The drug is reasonable and necessary for the treatment of the individual patient;
   - It is medically necessary that the drug be administered by an implanted infusion pump; and

The FDA approved labeling for the pump must specify that the drug being administered and the purpose for which it is administered is an indicated use for the pump.

**References**


Billing Coding/Physician Documentation Information

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>36260</td>
<td>Insertion of implantable intra-arterial infusion pump</td>
</tr>
<tr>
<td>36261</td>
<td>Revision of implantable intra-arterial infusion pump</td>
</tr>
<tr>
<td>36262</td>
<td>Removal of implanted intra-arterial infusion pump</td>
</tr>
<tr>
<td>36563</td>
<td>Insertion of tunneled centrally inserted central venous access device with subcutaneous pump</td>
</tr>
<tr>
<td>36575</td>
<td>Repair of tunneled or non-tunneled central venous access catheter, without subcutaneous port or pump, central or peripheral insertion site</td>
</tr>
<tr>
<td>36576</td>
<td>Repair of central venous access device, with subcutaneous port or pump, central or peripheral insertion site</td>
</tr>
<tr>
<td>36581</td>
<td>Replacement, complete, of a tunneled centrally inserted central venous catheter, without subcutaneous port or pump, through same venous access</td>
</tr>
<tr>
<td>36582</td>
<td>Replacement, complete, of a tunneled centrally inserted central venous access device, with subcutaneous port, through same venous access</td>
</tr>
<tr>
<td>36583</td>
<td>Replacement, complete, of a tunneled centrally inserted central venous access device, with subcutaneous pump, through same venous access</td>
</tr>
<tr>
<td>36584</td>
<td>Replacement, complete, of a peripherally inserted central venous catheter (PICC), without subcutaneous port or pump, through same venous access</td>
</tr>
<tr>
<td>36585</td>
<td>Replacement, complete, of a peripherally inserted central venous access device, with subcutaneous port, through same venous access</td>
</tr>
<tr>
<td>36590</td>
<td>Removal of tunneled central venous access device, with subcutaneous port or pump, central or peripheral insertion</td>
</tr>
<tr>
<td>61215</td>
<td>Insertion of subcutaneous reservoir, pump, or continuous infusion system for connection to ventricular catheter</td>
</tr>
<tr>
<td>62350</td>
<td>Implantation, revision or repositioning of tunneled intrathecal or epidural catheter, for long-term medication administration via an external pump or implantable reservoir/infusion pump; without laminectomy</td>
</tr>
<tr>
<td>62351</td>
<td>Implantation, revision or repositioning of tunneled intrathecal or epidural catheter, for long-term medication administration via an external pump or implantable reservoir/infusion pump; with laminectomy</td>
</tr>
<tr>
<td>62360</td>
<td>Implantation or replacement of device for Intrathecal or epidural drug infusion; subcutaneous reservoir</td>
</tr>
<tr>
<td>62361</td>
<td>Implantation or replacement of device for Intrathecal or epidural drug infusion;</td>
</tr>
</tbody>
</table>
subcutaneous reservoir – non programmable pump

62362 Implantation or replacement of device for Intrathecal or epidural drug infusion;

subcutaneous reservoir – programmable pump

62365 Removal of subcutaneous reservoir or pump, previously implanted for intrathecal or epidural infusion

62367 Electronic analysis of programmable, implanted pump for intrathecal or epidural drug infusion (includes evaluation of reservoir status, alarm status, drug prescription status); without reprogramming or refill

62368 Electronic analysis of programmable, implanted pump for intrathecal or epidural drug infusion (includes evaluation of reservoir status, alarm status, drug prescription status); with reprogramming

62369 Electronic analysis of programmable, implanted pump for intrathecal or epidural drug infusion (includes evaluation of reservoir status, alarm status, drug prescription status); with reprogramming and refill

62370 Electronic analysis of programmable, implanted pump for intrathecal or epidural drug infusion (includes evaluation of reservoir status, alarm status, drug prescription status); with reprogramming and refill (requiring a physician’s skill)

A4220 Refill kit for implantable infusion pump

A4221 Supplies for maintenance of drug infusion catheter, per week (list drug separately)

E0782 Infusion pump, implantable, non-programmable (includes all components, E.G., pump, catheter, connectors, etc.)

E0783 Infusion pump, implantable, programmable (includes all components, E.G., pump, catheter, connectors, etc.)

E0786 Implantable programmable infusion pump, replacement (excludes implantable intraspinal catheter)

Additional Policy Key Words
N/A

Policy Implementation/Update Information
1/1/88 New policy
6/1/00 No policy statement changes
6/1/01 Prior Authorization requirement added to the policy.
6/1/02 No policy statement changes
6/1/03 No policy statement changes
6/1/04 No policy statement changes, policy placed in Archives.
6/1/05 Policy removed from Archives. Prior authorization requirement statement removed from the policy.
6/1/06 No policy statement changes
6/1/07 No policy statement changes. Updated coding.
6/1/08 No policy statement changes.
6/1/09 No policy statement changes.
6/1/10 No policy statement changes.
10/1/10 First policy statement revised to indicate that, in order for implantable infusion pumps to be considered medically necessary for severe, chronic intractable pain, patients need to have had a successful trial of spinal opioid or non-opioid analgesics.
6/1/11 No policy statement changes.
1/1/12 Coding updated.
6/1/12 In medically necessary policy statement, fourth bullet point changed to say that a temporary trial of pain medication should use the same route of administration as the planned treatment.
6/1/13 Policy statements updated: Primary epithelial ovarian cancer (intraperitoneal infusion as component of chemotherapy) added as medically necessary. Head/neck cancers (intra-arterial injection of chemotherapeutic agents) changed to investigational.
6/1/14 Updated Regulatory Status w/latest info. No policy statement changes.
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